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Review Article

Natural Rescue and Resurgence of the Equine Corpus Luteum

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ABSTRACT

The recuperative powers of the equine corpus luteum (CL) are astonishing. The availability of transrectal ultrasonic imaging has led to three reports describing the rescue of the CL of the estrous cycle after the CL regressed to the dimensions and structure characteristic of the end of luteolysis. In two mares, a rescued CL increased in size and apparently in progesterone output during the postovulatory development of the CL of the next cycle or ensuing pregnancy. The other mare had a persistent CL (PCL). The CL from the ovulation at the beginning of the PCL decreased in area and in progesterone output to the size and function used to define the end of luteolysis. The transient regression occurred in the absence of a second ovulation or a follicle of preovulatory diameter but in the presence of an luteinizing hormone (LH) surge. Better known and documented is resurgence of the primary CL of pregnancy in cross-sectional area and progesterone output beginning on about 35 days after ovulation associated with the secretion of equine chorionic gonadotropin (eCG) from the developing endometrial cups. The demonstration of resurgence of the primary CL during pregnancy was preceded by about 40 years of misinformation and dogma about demise of the primary CL and replacement by secondary CL.

1. Introduction

The corpus luteum (CL) has profound hormonal power through production of progesterone (P4) and plays a pivotal role in animal reproductive biology. In cattle, natural resurgence of the CL is manifested as a rebound in P4 concentration about every 8 hours at the peak of each pulse of a metabolite of Prostaglandin F2α PGF2α) (PGFM) [1]. Before the beginning of luteolysis, the rebound returns P4 to the concentration before the PGFM pulse. During luteolysis, the rebound continues to occur but becomes progressively less effective in returning P4 to the pre-PGFM pulse concentration. When P4 has decreased to about half of its concentration during luteolysis, the rebound wanes. A P4 rebound after a pulse of PGFM has not been detected in mares [2,3]. Nevertheless, the primary equine CL of pregnancy undergoes well-documented natural resurgence in form and function beginning on about day 35 (day 0 = ovulation) [4,5]. Knowledge on the life span of the primary CL of equine pregnancy was subjected to misinterpretation and dogma for about 40 years until its life span was demonstrated by marking the CL with India ink [4].

This report describes rescue and resurgence of the CL in three mares: one for a CL of the interovulatory interval (IOI) during the next IOI (Section 3), one for the CL of an IOI during the ensuing pregnancy (Section 4), and one within the persistent CL (PCL) syndrome (Section 5). The P4 output of the rescued CL had decreased to near the experimental criterion used to define the end of the luteolytic period (a P4 decrease to 1 ng/mL in both heifers [6] and mares [7]). Reports for only three individual mares may indicate that

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CL rescue is rare, but like the discovery of many reproductive phenomena by transrectal ultrasonic imaging [8], awareness may lead to more frequent reports. The P4 rebound after the peak of a PGFM pulse in cattle is attributable in part to a pulse of luteinizing hormone (LH) (review [9]), and CL resurgence in pregnant mares is associated with the luteotropic properties of equine chorionic gonadotropin (eCG) from the endometrial cups (Section 4). Concentrations of LH were available for two of the three reports of CL rescue in mares, and each was temporally associated with a surge of LH. In this regard, treatment with pituitary antiserum, gonadotropins, gonadotropic releasing hormone, and in vitro culturing of luteal cells indicate that the equine CL requires circulating gonadotropins with luteotropic activity throughout diestrus and the corresponding days of early pregnancy (review [10]). Therefore, rescue and resurgence of the equine CL most likely represents luteotropic activity of LH or eCG.

2. Life of the Primary CL

Structure, echotexture [11], and function [9,10] of the CL in mares have been reviewed. Equine CL development occurs during about 5 days for the CL of an IOI, pregnancy, and PCL (Fig. 1). During CL development, P4 output progressively increases along with an increase in CL dimensions and vascularity and partial resorption and organization of a central blood clot (corpus hemorrhagicum). After the developmental stage, the next few days are characterized by a plateau in P4 output followed by a gradual but striking decline until about day 15 during both the IOI [12] and pregnancy [13,14]. Based on an inspection of published P4 profiles (n = 20 IOIs) [12], 40% of the P4 decrease occurred during a gradual decline between the maximum on day 8 and the beginning of luteolysis on day 15, and 60% occurred during the more abrupt decline of luteolysis. In the absence of luteolysis (pregnancy, PCL), the P4 concentration at the end of the gradual decline on day 15 is maintained until the beginning of resurgence of the CL of pregnancy on about day 35; a similar resurgence does not occur during the PCL syndrome.

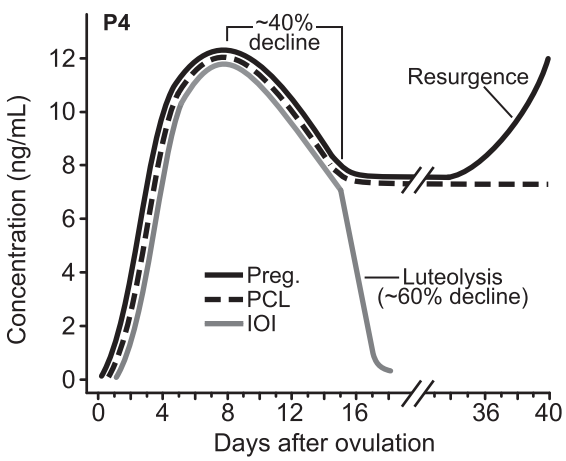

Fig. 1. Diagrammatic illustration of progesterone (P4) concentrations in mares during the first 40 days of pregnancy (Preg.) [13,14] and persistent corpus luteum (PCL) [7] and to the end of luteolysis of the interovulatory interval (IOI) [12], based primarily on the indicated publications.

The progressive decrease in P4 between about days 8–15 apparently has not been given specific attention or commentary but is a peculiarity of mares and occurs during the IOI, pregnancy, and PCL. In contrast, P4 continues to increase until luteolysis begins in heifers and/or cows, providing a species comparison that should be of interest to biologists [9]. After the gradual P4 decrease in mares during the IOI, the P4 decrease becomes more abrupt (luteolysis). When blood sampling is done infrequently (e.g., every 6 hours, daily), the process of luteolysis is depicted as requiring 2 or 3 days. This is an illusion, owing to the beginning and end of luteolysis at different times in individuals [15]. Hourly sampling has shown a mean length of luteolysis of 23 hours in mares [16] and 24 hours in heifers [1], using 1.0 ng/mL as an indicator of the end of luteolysis [7]. The P4 concentration, however, slowly continues to decrease. In three mares with available hourly data, P4 decreased from 0.9 to 0.1 ng/mL in 22–32 hours [16].

3. Rescue of the CL of IOI with Partial Resurgence During the Next IOI

The rescue of the CL of an IOI (CL1) and its partial resurgence during the life of the CL of the next IOI (CL2) has been observed. The study included daily blood sampling for P4 concentration throughout the two IOIs and CL dimensions and blood flow of each of CL1 and CL2. Concentration of P4 appeared to decrease in the expected manner that otherwise would have defined the end of luteolysis to a minimal concentration on day 17 (Fig. 2). The P4 then increased slowly to a concentration of 3 ng/mL on day 23 or the day of ovulation at the end of the IOI and beginning of the next IOI. The percentage of CL1 with blood flow signals and CL area (cm^2) reached nadirs on days 18 and 21, respectively, indicating the beginning of rescue.

Cross-sectional area and blood flow of CL1 fluctuated considerably during the next IOI. A marked increase in blood flow of CL1 began 3 days before the apparent increase in CL area (cm^2). The values for area and blood flow of the rescued CL1 were about half of the values for CL2 during days 0–8 and days 2–9, respectively. Based on intraovarian location of the CL, ultrasonic appearance of the CL, and failure to detect another CL or luteinized follicle in the vicinity of the CL, the operator was convinced that the same CL (CL1) was being followed; the CL from the ovulation at the beginning of the next IOI (CL2) was in the opposite ovary. The ovulatory LH surge for the second ovulation began on day 17 of the first IOI. The surge therefore encompassed the rescue of CL1 and was the likely luteotropic source for CL rescue. Although a mental stretch, the transient 2-day increase in P4 shown (Fig. 2) at the decrease in the area of CL2 may have represented a delayed decrease in the area of CL1. Rescue of CL1 when it was near the definition of the end of luteolysis followed by partial resurgence seems difficult to believe but is also difficult to refute. Confirmation of the rescue phenomenon and experimental rescue is needed.